## REMARKS

Reconsideration of the rejections set forth in the Office action mailed November 2, 2005 is respectfully requested. Claims 23-31 are pending. Claims 28-31 are under examination, claims 32-33 have been cancelled, and claims 23-27 are currently withdrawn from consideration.

### I. Amendments

Claim 28 is amended to recite "said first end sequence and said second end sequence" in place of "said first and second end sequences", so that explicit antecedent support is provided.

Claim 28 is also amended, for emphasis, to state that the end sequences are ligated "directly" together.

Claim 28 is also amended to more particularly point out the features of the invention, by reciting that each end sequence in the plurality of oligonucleotides is unique. Support is found, for example, at page 7, lines 18-35. See, for example, lines 24-25 ("...the number of nucleotides determined could be as low as five or six, and still have a significant probability that each end sequence would be unique"), and 27-28 ("for polynucleotides less than or equal to 10 megabases, 9-12 nucleotides are preferably determined to ensure that the end sequences are unique"). This feature ensures that each end sequence is effective to uniquely identify the restriction fragment from which it was derived. See e.g. page 9, lines 31-33: "In a polynucleotide having a random sequence of nucleotides, a 9-mer appears on average about once every 262,000 bases. Thus, 9-mer sequences are quite suitable for uniquely labeling restriction fragments...".

Claim 32 is cancelled.

No new matter is added by any of the amendments.

### II. Rejections under 35 U.S.C. §112, Second Paragraph

Claim 28 was rejected under 35 U.S.C. §112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 28 has been amended to recite "said first end sequence and said second end

sequence" in place of "said first and second end sequences", so that explicit antecedent support is provided.

In view of the foregoing, the applicants submit that amended claim 28 complies with the requirements of 35 U.S.C. §112, second paragraph.

III. Rejections under 35 U.S.C. §102(b)

Independent claim 28 and its dependent claims were rejected under 35 U.S.C. §102(b) as being anticipated by New England Biolabs 96/97 Catalog, pages 19, 37, 108 and 109. This rejection is respectfully traversed for the following reasons.

A. The Claims

Independent claim 28 recites a plurality of oligonucleotides derived from restriction fragments of a polynucleotide, each said oligonucleotide containing first and second end segments from opposite ends of one such restriction fragment, wherein

said first end segment consists of a first end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

said second end segment consists of a second end sequence, having 5 to 12 basepairs, immediately adjacent to a cleaved restriction site,

and said first end sequence and said second end sequence are ligated directly together;

wherein each end sequence contains the same number of basepairs;

and wherein each end sequence in the plurality of oligonucleotides is unique.

B. The Prior Art

The Examiner refers in particular to a primer on page 109 of the cited catalog, having the following sequence: 5'd(**ATTGTTG**CCGGGAAGCTAGAGTA**AGTAGTT**)3', where the underlined regions are restriction enzyme recognition sites. The boldfaced areas are stated by the Examiner to represent the same-length "end sequences" of the claim.

This structure does not meet the limitations of independent claim 28, for at least the following reasons.

As stated above, claim 28 recites that each "end sequence" is "immediately adjacent to a cleaved restriction site", and that "said first end sequence and said second end sequence are ligated directly together".

(1) The restriction sites in the cited structure are not cleaved restriction sites.

(2) The "end sequence" **AGTAGTT** is not "immediately adjacent" to the CTAG restriction site, whether it is cleaved or uncleaved. It is unclear to the applicant how two sequences that are four nucleotides apart could be considered "immediately adjacent".

(3) In the prior art structure, the first "end sequence" **ATTGTTG** and the second "end sequence" **AGTAGTT** are not ligated together, but rather are separated by a sequence of sixteen nucleotides.

Point (3) was actually addressed in the previous response, filed August 17, 2005, in addressing the reference Morgante *et al.*:

> "Morgante *et al.* teach the ligation of synthetic oligonucleotide adaptors to the ends of DNA restriction fragments.... the adaptors are not ligated to each other, but to both ends of a DNA fragment.
>
> The Examiner asserts that the claims as previously presented did not require that the pair of ligated sequence tags (now termed end sequences) be directly connected to each other (page 7 of Office Action).
>
> The independent claim as amended now clearly recites that "said first and second end sequences are ligated together"."

It is the applicant's view that two sequences that are separated by sixteen nucleotides, as in the prior art structure, would not be considered "ligated together", especially by one skilled in the art. Nonetheless, the claim has been amended, for emphasis, to state that the end sequences are ligated "directly" together.

The cited reference clearly does not disclose all of the elements set out above in claim 28 and inherently present in dependent claims 29-33. Accordingly, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

IV. Further Rejections under 35 U.S.C. §102(b)

Independent claim 28 and its dependent claims were rejected under 35 U.S.C. §102(b) as being anticipated by Howard *et al.*, *BioTechniques* 7:940-2 (1989).

A. The Claims

The subject matter of independent claim 28 is described above.

B. The Prior Art

The Examiner specifically refers to the vector shown in "Table 1" of the reference, which has the following sequence:

5'-**GAATTC**GCGGCCGCCATGGAGATCTCGAGGCCTATCGATCCGCGG**AAGCTT**-3',

where the underlined regions are restriction enzyme cleavage sites. The boldfaced areas are stated by the Examiner to represent the same-length "end sequences" of the claim.

This structure does not meet the limitations of claim 28, for at least the following reasons.

Claim 28 recites that each "end sequence" is "immediately adjacent to a cleaved restriction site", and that "said first end sequence and said second end sequence are ligated directly together".

(1) The restriction sites in the structure are not cleaved restriction sites.

(2) In the prior art structure, the first "end sequence" **GAATTC** and the second "end sequence" **AAGCTT** are separated by a sequence of 33 nucleotides. It is unclear to the applicant how two segments that are separated by 33 nucleotides could be considered "ligated together", much less "ligated directly together".

The reference does not disclose all of the elements set out above in claim 28 and its dependent claims 29-33. In view of this, the applicant respectfully requests the Examiner to withdraw the rejection under 35 U.S.C. §102(b).

V. Conclusion

Applicant would like to note that this is the fourth response filed in this application, and that the current Office Action appeared to raise issues that had been addressed earlier in prosecution, as noted above. Moreover, the assertion regarding claim 32 on page 4 of the

Office Action, though moot in view of the cancellation of this claim, referred to claim language ("having a size") which had been removed by amendment earlier in prosecution. Applicant respectfully requests more expedited prosecution of the claims.

In view of the foregoing, the applicant submits that the claims under examination are in condition for allowance. A Notice of Allowance is, therefore, respectfully requested.

If in the opinion of the Examiner a telephone conference would expedite the prosecution of the subject application, the Examiner is encouraged to call the undersigned at (650) 838-4403.

Respectfully submitted,

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